

TOWNSEND and TOWNSEND and CREW LLP

By: _____

Lillian M. Montano

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Gerald Koelsch, et al.

Application No.: 10/773,754

Filed: February 6, 2004

For: INHIBITORS OF MEMAPSIN 2
AND USE THEREOF

Confirmation No.: 5585

Examiner: Suzanne Marie Noakes

Art Unit: 1653

INFORMATION DISCLOSURE
STATEMENT UNDER 37 CFR §1.97 and
§1.98

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The references cited on attached form PTO/SB/08B are being called to the attention of the Examiner. This application is a continuation of and relies on U.S. Patent Application No. 09/845,226, filed April 30, 2001 (Attorney Docket No. 022266-000920US), which is a divisional of and relies on U.S. Patent Application No. 09/603,713, filed June 27, 2000 (Attorney Docket No. 022266-000910US) for an earlier effective filing date under 37 U.S.C. §120. In accordance with 37 CFR §1.98(d), copies of those references that have been previously submitted to or cited by the Patent Office in the parent applications are not enclosed. Copies of references FK-FL have not been previously cited, and are therefore enclosed.

Further, Applicants attach a copy of an Australian Examination Report dated June 26, 2006, which was issued in counterpart Australian application No. 2004202058, and in which references FK-FL were cited.

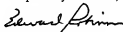
It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

This IDS is being filed before the mailing date of the final Office Action or Notice of Allowance.

Please charge the IDS fee of \$180 to Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



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Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet **3** of **11****Complete if Known**

Application Number	10/820,953
Filing Date	April 4, 2004
First Named Inventor	Jordan J.N. Tang
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	022268-000840US

U.S. PATENT DOCUMENTS*

Examiner Initials ¹	Cite No. ¹	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
	AA	US-4,523,957		05/08/90	Bobbitt, et al.	
	AB	US-5,221,607		06/22/93	Cordell, et al.	
	AC	US-5,252,463		10/12/93	Nelson, et al.	
	AD	US-5,235,043		06/10/93	Collins, et al.	
	AE	US-5,744,345		04/28/98	Chrysler, et al.	
	AF	US-6,207,710 B1		03/27/01	Acosta, et al.	
	AG	US-6,245,884 B1		06/12/01	Hook	
	AH	US-6,281,223 B1		09/18/01	Christie, et al.	
	AI	US-6,313,266 B1		11/06/01	Hook	
	AJ	US-6,319,660 B1		11/20/01	Powell, et al.	
	AK	US-6,328,163 B1		12/11/01	Anderson, et al.	
	AL	US-6,361,975 B1		03/29/02	Christie, et al.	
	AM	US-6,420,634 B1		07/18/02	Gurney, et al.	
	AN	US-6,545,127		04/08/03	Teng, et al.	
	AO	US-2002/0081834 A1		07/18/02	Gurney, et al.	
	AP	US-2002/0050459 A1		05/09/02	Chopra, et al.	
	AQ	US-2002/0072050 A1		06/13/02	Hook	
	AR	US-2002/0037310 A1		03/25/02	Gurney, et al.	
	AS	US-2002/0159991 A1		10/31/02	Cordell, et al.	
	AT	US-2002/0157122 A1		10/24/02	Wong, et al.	
	AU	US-				

FOREIGN PATENT DOCUMENTS

Examiner Initials ¹	Cite No. ¹	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁴
		Country Code ³	Number ¹	Kind Code ² (if known)				
	AV	WO	96/40885	A2	12/19/96			<input type="checkbox"/>
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	AZ	WO	98/21588	A1	05/22/98			<input type="checkbox"/>
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	BB	WO	98/51752	A1	10/14/99			<input type="checkbox"/>
	BC	WO	98/64587	A1	12/16/99			<input type="checkbox"/>
	BD	WO	00/17369	A3	03/30/00			<input type="checkbox"/>
	BE	WO	00/23576	A3	04/27/00			<input type="checkbox"/>
	BF	WO	00/47618	A2	08/17/00			<input type="checkbox"/>
	BG	WO	00/58479	A1	10/05/00			<input type="checkbox"/>
	BH	WO	00/77030	A1	12/21/00			<input type="checkbox"/>

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¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet **4** of **11****Complete if Known**

Application Number	10/820,953
Filing Date	April 4, 2004
First Named Inventor	Jordan J.N. Tang
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	022256-000940US

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ²
		Country Code ³	Number ⁴	Kind Code ⁵ (if known)				
	BI	WO	01/23533	A2	04/05/01			<input type="checkbox"/>
	BJ	WO	01/70672	A1	09/27/01			<input type="checkbox"/>
	BK	WO	02/47466	A2	06/20/02			<input type="checkbox"/>
	BL	WO	02/25276	A1	03/28/02			<input type="checkbox"/>
	BM	EP	0855444	A2	07/29/86			<input type="checkbox"/>
	BN	EP	0302469	A2	02/08/89			<input type="checkbox"/>
	BO	JP	10106681	A	04/28/88			<input type="checkbox"/>

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Substitute for form 1449B/PTO		Complete if Known			
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	10/820,953		
		Filing Date	April 4, 2004		
		First Named Inventor	Jordan J.N. Tang		
		Art Unit	Not Yet Assigned		
		Examiner Name	Not Yet Assigned		
Sheet	5	of	11	Attorney Docket Number	022266-000840US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	BP	ABAD-ZAPATERO et al., "Structure of a secreted aspartic protease from <i>C. albicans</i> complexed with a potent inhibitor: implications for the design of antifungal agents," <i>Protein Sci</i> 9(4):640-52 (1996).	
	BQ	ABBENATE, et al., "Inhibitors of β -amyloid formation based on the β -secretase cleavage site," <i>Biochemical and Biophysical Research Communications</i> 268(1):133-136 (2000).	
	BR	ASKEVI, et al., "Molecular recognition with convergent functional groups. Synthetic and structural studies with a model receptor for nucleic acid components," <i>J. Am. Chem. Soc.</i> 111:1082-1090 (1989).	
	BS	ADAMS, M.D., et al., JP10108681A/GaHespin K Gene Abstract. MicroPatent Bibliographic Database [Online]. Retrieved from the Internet - <URL: http://www.micropat.com/itabcs/com.../misc.005877274/JP10108681.html >	
	BT	BAILEY & COOPER, "A structural comparison of 21 inhibitor complexes of the aspartic proteinase from <i>Endothia parasitica</i> ," <i>Protein Sci</i> 3(11):2129-43 (1994).	
	BU	BRUNGER, et al., "Crystallography & NMR system: A new software suite for macromolecular structure determination," <i>Acta Crystallogr B</i> 46 Pt 8:905-21 (1990).	
	BV	CAPELL, et al., "The proteolytic fragments of the Alzheimer's disease-associated presenilin-1 form heterodimers and occur as a 100-150-kDa molecular mass complex," <i>J Biol Chem</i> 273(8):3205-11 (1998).	
	BW	CHARTIER-HARLIN, et al., "Early-onset Alzheimer's disease caused by mutations at codon 717 of the beta-amyloid precursor protein gene," <i>Nature</i> 353(6347):844-8 (1991).	
	BX	CITRON, et al., "Mutation of the beta-amyloid precursor protein in familial Alzheimer's disease increases beta-protein production," <i>Nature</i> 360(6408):672-4 (1992).	
	BY	COHEN, et al., "An artificial cell-cycle inhibitor isolated from a combinatorial library," <i>Proc Natl Acad Sci USA</i> 95(24):14272-7 (1998).	
	BZ	CORDER, et al., "Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's DISEASE in late onset families," <i>Science</i> 281(5323):921-3 (1995).	
	CA	COWLEY, et al., "Alzheimer's: unlocking the mystery," <i>Newsweek</i> January 31, 2000.	
	CB	CUTFIELD, et al., "The crystal structure of a major secreted aspartic proteinase from <i>Candida albicans</i> in complexes with two inhibitors," <i>Structure</i> 3(11):1281-71 (1995).	
	CC	DAVIES, "The structure and function of the aspartic proteinases," <i>Annu Rev Biophys Chem</i> 9:189-216 (1990).	
	CD	DEALWIS, et al., "X-ray analysis at 2.0 Å resolution of mouse submaxillary renin complexed with a decapeptide inhibitor CH-66, based on the 4-16 fragment of rat angiotensinogen," <i>J. Mol. Biol.</i> 236(1):342-50 (1994).	
	CE	DE STROOPER, et al., "Deficiency of presenilin-1 inhibits the normal cleavage of amyloid precursor protein," <i>Nature</i> 391(6665):387-90 (1998).	

Examiner Signature	Date Considered
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*EXAMINER: Initial reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet	6	of	11	Application Number	10/820,953
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Complete if Known

Application Number	10/820,953
Filing Date	April 4, 2004
First Named Inventor	Jordan J.N. Tang
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	022266-000940US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	CF	DORRELL, S "Unfurling Alzheimer's Disease with β -secretase inhibitors." <i>Drug Discovery Today</i> , 5(8):316-317 (2000).	
	CG	DURN, Structure and Functions of the Aspartic Proteinases, Adv. In Exptl. Med. Biol. 306 (Plenum Press, NY 1991).	
	CH	ELLINGTON & SZOSTAK, "In vitro selection of RNA molecules that bind specific ligands," <i>Nature</i> 346(6267) 818-22 (1999).	
	CI	ERMOLIEFF et al., "Proteolytic activation of recombinant Pro-memapsin 2 (Pro- β -secretase) studied, with new fluorogenic substrates," <i>Biochemistry</i> 39(40), 12450-12458 (2000).	
	CJ	EZZELL, C., "Alzheimer's Alchemy," <i>Science News</i> (1992) 141:152-153	
	CK	FAN, et al., "BACE Maps to chromosome 11 and a BACE homolog, BACE2, resides in the obligate down syndrome region of chromosome 21," <i>Science</i> 265:255a (1999).	
	CL	FIELDS & SONG, "A novel genetic system to detect protein-protein interactions," <i>Nature</i> 340(6230):245-8 (1999).	
	CM	GHOSH & FIDANZE, Transition-state mimetics for HIV protease inhibitors. Stereoccontrolled synthesis of hydroxyethylene and hydroxyethylamine isosteres by ester-derived titanium enolates syn and anti-add reactions," <i>Org. Chem.</i> 63:9148-54 (1998).	
	CN	GHOSH, A.K. et al., "Structure-Based Design: Potent Inhibitors of Human Brain Memapsin 2 (β -Secretase)," <i>J. Med. Chem.</i> 44:2885-2888 (2001).	
	CO	GHOSH et al., "Design of potent inhibitors for human brain memapsin 2 (β -secretase)," <i>J. Am Chem Soc</i> 122(14):3522-3523 (2000).	
	CP	GLENNER & WONG, "Alzheimer's disease: Initial report of the purification and characterization of a novel cerebral/vascular amyloid protein," <i>Biochem Biophys Res Commun</i> 120(3):885-90 (1984)	
	CQ	GOATE, et al., "Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease," <i>Nature</i> 346(6311):704-6 (1991).	
	CR	GOLDGABER, et al., "Characterization and chromosomal localization of a cDNA encoding brain amyloid of Alzheimer's disease," <i>Science</i> 235(4791):877-80 (1987).	
	CS	GURNEY, M.E. et al., "U.S. Published Patent Application, US 2002/0037315 A1," published Mar. 28, 2002, filing date Feb. 27, 2001.	
	CT	HAASS & DE STROOPER, "The presentins in Alzheimer's disease—Proteolysis holds the key," <i>Science</i> 266:916-918 (1999).	
	CU	HONG et al, "Structure of the protease domain of memapsin 2 (β -secretase) complexed with inhibitor," <i>Science</i> 290:150-153 (2000).	

Examiner Signature	Date Considered
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* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 7 of 11**Complete if Known**

Application Number	10/820,953
Filing Date	April 4, 2004
First Named Inventor	Jordan J.N. Tang
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	022268-000940US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	CV	HOWLETT, D.R. et al., "In search of an enzyme: the β -secretase of Alzheimer's disease is an aspartic proteinase," <i>Trends Neurosci.</i> 23:565-570 (2000)	
	CW	JAMES, Aspartic Proteinases, Retroviral and Cellular Enzymes, Adv. In Exptl. Med. Biol. 438 (Plenum Press, NY 1995).	
	CX	JONES, et al., "Improved methods for binding protein models in electron density maps and the location of errors in these models," <i>Acta Crystallogr A</i> 47 (Pt 2): 110-9 (1991).	
	CY	JORM, ed., <i>A Guide to the Understanding of Alzheimer's Disease and Related Disorders</i> (New York University Press, New York 1987).	
	CZ	KANG, et al., "The precursor of Alzheimer's disease amyloid A β protein resembles a cell-surface receptor," <i>Nature</i> 325(6106):733-6 (1987).	
	DA	KEARNEY & AWEEKA, "The penetration of anti-infectives into the central nervous system," <i>Neurol. Clin.</i> 17(4):883-900 (1999).	
	DB	KELLY & DOW, "Microbial differentiation: the role of cellular asymmetry," <i>Microbiol Sci</i> 1:214-6 (1984).	
	DC	KHAN, et al., "Lowering the entropic barrier for binding conformationally flexible inhibitors to enzymes," <i>Biochemistry</i> 37(46):15639-45 (1998).	
	DD	KNOPS, et al., "Cell-type and amyloid precursor protein-type specific inhibition of A β release by bafilomycin A1, a selective inhibitor of vacuolar ATPases," <i>J Biol Chem</i> 270(6):2419-22 (1995).	
	DE	KOLATA, "Scientists find enzyme linked to Alzheimer's," <i>National Science/Health</i> October 22, 1999.	
	DF	KOSTKA, <i>Aspartic proteinases and Their Inhibitor</i> (Walter de Gruyter, Berlin 1985).	
	DG	LASKOWSKI, et al., "Procheck: a program to check the stereochemical quality of protein structures," <i>J Appl. Crystallog</i> 26:283 (1993).	
	DH	LEMAIRE, et al., "The ProA β (95) precursor protein of Alzheimer's disease A β amyloid is encoded by 16 exons," <i>Nucleic Acids Res</i> 17(2):517-22 (1989).	
	DI	LEVY, et al., "Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral hemorrhage, Dutch type," <i>Science</i> 244(4859):1124-6 (1990).	
	DJ	LEVY-LAHAD, et al., "Candidate gene for the chromosome 1 familial Alzheimer's disease locus," <i>Science</i> 269(5228):973-7 (1995).	
	DK	LEWIS & DEAN, "Automated site-directed drug design: the concept of spacer skeletons for primary structure generation," <i>Proc R Soc Lond B Biol Sci</i> 236(1283):125-49 and 141-162 (1989).	

Examiner
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Sheet	8	of	11	Application Number	10/820,953
				Filing Date	April 4, 2004
				First Named Inventor	Jordan J.N. Tang
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	022286-000940US

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	DL	LIU, et al., "Intracellular division of glycoprotein GP 160 of human immunodeficiency virus to lysosomes as a strategy of AIDS gene therapy," <i>FASEB J</i> 7(11):1070-80 (1993).	
	DM	LIU et al., "Human aspartic protease memapsin 2 cleaves the β -secretase site of β -amyloid precursor protein," <i>PNAS</i> 97(4):1456-1460 (2000).	
	DN	MAJER, P. et al., "Structure-based subsite specificity mapping of human cathepsin D using statine-based inhibitors," <i>Protein Science</i> , 6(7):1456-1466 (1997).	
	DO	NANN, "Cerebral amyloidosis, aging and Alzheimer's disease; a contribution from studies on Down's syndrome," <i>Neurobiol Aging</i> 10(5):397-9 (1989).	
	DP	MARCINISZYN, et al., "Mode of inhibition of acid proteases by pepstatin," <i>J Biol. Chem.</i> 251(22):7088-94 (1976).	
	DQ	MARTSON, F.A.C. et al., "Solubilization of protein aggregates," <i>Methods of Enzymology</i> , 162:264-278 (1990).	
	DR	MATSUMOTO, et al., "Molecular cloning of human cDNA with a sequence highly similar to that of the dihydrofolate reductase gene in brain libraries derived from Alzheimer's patients," <i>Eur. J. Biochem.</i> 230:337-343 (1995).	
	DS	MECKELEIN, et al., "Identification of a novel serine protease-like molecule in human brain," <i>Molecular Brain Research</i> 55:181-197 (1998).	
	DT	MCKINLAY & ROSSMANN, "Rational design of antiviral agents," <i>Annu Rev Pharmacol Toxicol</i> 29:111-22 (1989).	
	DU	MULLAN, et al., "A locus for familial early-onset Alzheimer's disease on the long arm of chromosome 14, proximal to the alpha 1-antichymotrypsin gene," <i>Nat Genet</i> 2(4):340-2 (1992).	
	DV	MULLAN, et al., "A pathogenic mutation for probable Alzheimer's disease in the APP gene at the N-terminus of beta-amyloid," <i>Nat Genet</i> 1(8):345-7 (1992).	
	DW	MURRELL, et al., "A mutation in the amyloid precursor protein associated with hereditary Alzheimer's disease," <i>Science</i> 254(5028):97-9 (1991).	
	DX	NAVAZA, "AMoRe: an automated package for molecular replacement," <i>Acta Crystallogr Sect A</i> 50:157 (1997).	
	DY	OEFFNER, C. et al., "Renin inhibition by substituted piperidines: A novel paradigm for the inhibition of monomeric aspartic proteases?" <i>Chemistry & Biology</i> (London), 6(3):127-131 (1999).	
	DZ	OTWINOWSKI & MINOR, "Processing of X-ray diffraction data collected in Oscillation mode," <i>Methods Enzymol</i> 276:307 (1997).	
		PARIS, N. et al., "Bacterial Production and Purification of Recombinant Human Prolactin," <i>Biotechnology and Applied Biochemistry</i> , 12:436-449 (1990).	

Examiner
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				Filing Date	April 4, 2004
				First Named Inventor	Jordan J.N. Tang
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	022268-000640US

Complete if Known**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials *	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	EA	PEREZ, et al., "Enhanced release of amyloid beta-protein from codon 670/671 "Swedish" mutant beta-amyloid precursor protein occurs in both secretory and endocytic pathways," <i>J Biol Chem</i> 271(18):9106-7 (1996)	
	EB	PERRY & DAVIES, QSAR: Quantitative Structure-Activity Relationships in Drug Design pp. 169-193 (Alan R. Liss, inc. 1999)	
	EC	PHIMISTER, "Four companies announce discovery of b-secretase gene," <i>Nature Biotechnology</i> 18:16 (2000).	
	ED	PODLISNY, et al., "Presenilin proteins undergo heterogeneous endoproteolysis between Thr291 and A16269 and occur as stable N- and C-terminal fragments in normal and Alzheimer brain tissue," <i>Neurobiol Dis</i> 3(4):325-37 (1997)	
	EE	RIPKA, "Computers picture the perfect drug," <i>New Scientist</i> 54-57 (1996)	
	EF	ROBAKIS, et al., "Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides," <i>Proc Natl Acad Sci U S A</i> 84(12):4190-4 (1987).	
	EG	ROBERTS & SZOSTAK, "RNA-peptide fusions for the in vitro selection of peptides and proteins," <i>Proc Natl Acad Sci U S A</i> 94(23):12297-302 (1997).	
	EH	ROGAIEV, et al., "Familial Alzheimer's disease in kindreds with missense mutations in a gene on a chromosome 1 related to the Alzheimer's disease type 3 gene," <i>Nature</i> 376(6543):775-8 (1995).	
	EI	ROTELLO, D.P., "Fenchylamine Sulfonamide Inhibitors of Amyloid β -Peptide Production by the γ -Secretase Proteolytic Pathway: Potential Small Molecule Therapeutic Agents for the Treatment of Alzheimer's Disease," <i>Chemtracts - Organic Chemistry</i> 13:828-829 (2000).	
	EJ	ROUVINEN, et al., "Computer aided drug design," <i>Acta Pharmaceutica Fennica</i> 97, 159-166 (1998).	
	EK	RUMBLE, et al., "Amyloid A4 protein and its precursor in Down's syndrome and Alzheimer's disease," <i>N Engl J Med</i> 320(22):1445-52 (1989).	
	EL	SELKOE, et al., "Transferring cell biology into therapeutic advances in Alzheimer's disease," <i>Nature</i> 399(6736 Suppl):A23-31 (1999).	
	EM	SHERRINGTON, et al., "Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease," <i>Nature</i> 376(6534):754-60 (1995).	
	EN	SINHA & LIEBERBURG, "Cellular mechanisms of beta-amyloid production and secretion," <i>Proc Natl Acad Sci U S A</i> 96(20):11046-53 (1999).	
	EO	SINHA, et al., "Purification and cloning of amyloid precursor protein beta-secretase from human brain," <i>Nature</i> 402(6781):537-40 (1999).	
	EP	STEINER, et al., "Expression of Alzheimer's disease-associated presenilin-1 is controlled by proteolytic degradation and complex formation," <i>J Biol Chem</i> 273(48):32322-31 (1998).	

Examiner Signature	Date Considered
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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet **10** of **11****Complete if Known**

Application Number	10/820,953
Filing Date	April 4, 2004
First Named Inventor	Jordan J.N. Tang
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	022266-000940US

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	EQ	SUZUKI, et al., "An increased percentage of long amyloid beta protein secreted by familial amyloid beta protein precursor (beta APP717) mutants," <i>Science</i> 264(5163) 1336-40	
	ER	SYMERSKY, et al., "High-resolution structure of the extracellular aspartic protease from <i>Candida tropicalis</i> yeast," <i>Biochemistry</i> 36(42):12700-10 (1997)	
	ES	SZOSTAK, "In vitro genetics," <i>TIBS</i> 18:68 (1992)	
	ET	TAGAWA, et al., "Alzheimer's disease amyloid β -clipping enzyme (APP secretase): Identification, purification, and characterization of the enzyme," <i>Biochemical and Biophysical Research Communications</i> 177(1):377-387 (1991).	
	EU	TAKAHASHI, Aspartic Proteases, Structure, Function, Biology, Biomedical Implications, <i>Adv. in Exptl. Med. Biol.</i> 382 (Plenum Press, NY 1995).	
	EV	TANG, Acid Proteases, Structure, Function and Biology, <i>Adv. in Exptl. Med. Biol.</i> vol. 95 (Plenum Press, NY 1977)	
	EW	TANG, et al., "Structural evidence for gene duplication in the evolution of the acid α s," <i>Nature</i> 271(5646):616-21 (1978)	
	EX	TANZI, et al., "Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease," <i>Nature</i> 331(6156):528-30 (1988).	
	EY	The early story of Alzheimer's Disease, edited by Bick et al. (Raven Press, New York 1987)	
	EZ	THINAKARAN, et al., "Endoproteolysis of presenilin 1 and accumulation of processed derivatives in vivo," <i>Neuron</i> 17(1):181-90 (1996).	
	FA	THINAKARAN, et al., "Evidence that levels of presenilins (PS1 and PS2) are coordinately regulated by competition for limiting cellular factors," <i>J Biol Chem</i> 272(45):28415-22 (1997).	
	FB	THINAKARAN, et al., "Stable association of presenilin derivatives and absence of presenilin interactions with APP," <i>Neurobiol Dis</i> 4(6):438-53 (1998)	
	FC	TURNER et al., "Substrate specificity of momepsin 2 (β -secretase): basis for inhibitor drug designed for Alzheimer's disease," <i>Experimental Biology 2001</i> at FASEB Office of Scientific March 31-April 4, 2001, Orlando, Florida. (Abstract)	
	FD	VAN BROECKHOVEN, et al., "Amyloid beta protein precursor gene and hereditary cerebral hemorrhage with amyloidosis (Dutch)," <i>Science</i> 248(4958):1120-2 (1990).	
	FE	VARON, S., et al., "Neurotrophic and Neurite Promoting Factors and Their Clinical Potentials", <i>Dev. Neurosci</i> (1993/94) 6:73-100	
	FF	VASSAR, et al., "Beta-secretase cleavage of Alzheimer's amyloid precursor protein by the transmembrane aspartic protease BACE," <i>Science</i> 259(5446):735-41 (1999).	

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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 808. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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**INFORMATION DISCLOSURE
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Sheet 11

of 11

Complete if Known

Application Number	10/820,953
Filing Date	April 4, 2004
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Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	022286-000940US

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	FG	WOLFE, et al., "Two transmembrane aspartates in presenilin-1 required for presenilin endoproteolysis and gamma-secretase activity," <i>Nature</i> 398(6727):513-7 (1999).	
	PH	YANG & QUAIL, "Structure of the Rhizomucor michei aspartic proteinase complexed with inhibitor pepstatin A at 2.7 Å resolution," <i>Acta Crystallogr D Biol Crystallogr</i> 55 (Pt 3):626-30 (1999)	
	FI	YOSHIKAI, et al., "Genomic organization of the human amyloid beta-protein precursor gene," <i>Gene</i> 87(2) 267-63 (1995).	
	FJ	YU, "Inhibition of beta-amyloid cytotoxicity by minkins," <i>Neurosci Lett</i> 254(3),125-8 (1998).	
	FK	Database Swissprot, Database Accession No. P28712, December 1, 1992	
	FL	Database Swissprot, Database Accession No. P56272, July 15, 1998	

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